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RE: ***Please see attached.***

#12 BD 4-22-03

Perkins Coie

April 21, 2003

TO: Examiner Deborah Crouch and Examiner Thái-An Ton

Art Unite: 1632

FROM: James J. Zhu, Reg. No. 52, 396

RE: **Issues to be discussed for a phone interview scheduled at 10:30 am (PST), 24 April 2003, between Applicant and Examiners regarding the Final Office Action, dated 11 February 2003, for "A Method and System for Introducing A Gene into A Human Stem Cell," Application No. 09/781,046.**

Applicant appreciates that a phone interview is allowed and scheduled at 10:30 am, 24 April 2003, to discuss the Final Office Action regarding the above captioned application.

The Final Office Action, dated February 11, 2003, rejects claims 22-26 for being not enabling under 35 U.S.C. 112. In particular, the Office Action asserts that 1) the Written Assurance Statement is unclear and 2) it would have required undue experimentation for one skilled in the art to expect that the sperm-specific antibodies of the present invention would retain the ability to fertilize an oocyte.

For the sake of expediting the phone interview process, Applicant highlights issues to be discussed as follows:

I. It would not require undue experimentation to make and/or use the claimed antibodies.

a. Some of antisperm antibodies do not cause infertility.

The Final Office Action's rejection is premised on showings in the art of immunocentraception that certain antibodies bound to the surface of sperm cells inhibit fertilization. *See* Yan *et al.*, Nakamura *et al*, Naz *et al.*, Kim *et al.*, all cited in a prior Office Action dated 28 August 2002. The Final Office Action also quotes a statement from Nakamura *et al* teaching that "it is believed that antisperm antibodies cause infertility in some male and female patients". The Final Office Action then concludes that "in general antibodies directed to sperm would be expected to inhibit fertilization".

Recent studies, however, have shown the contrary. For example, it has been reported that sera from all men contain antisperm antibodies but clearly some of antisperm antibodies do not cause infertility. Chiu & Chamley, Use of Antisperm Antibodies in Differential Display Western Blotting to identify Sperm Proteins Important in Fertility, *Hum. Reprod.* 17: 984-989 (2002) (See Abstract of this paper attached hereto). Chiu and Chamley have also demonstrated that an antibody binds to a sperm cell by a non-antigenic mechanism and the sperm cell bound with the antibody is a normal motile sperm. Id. In other words, not all sperm-specific antibodies would be expected to inhibit fertilization and actually some of the antibodies would not inhibit fertilization.

b. Applicant tracks the rulings of *In re Wands.*

In Wands, 858 F.2d 731 (1988), the claimed invention was directed to a method for immunoassay of HBsAg by using high-affinity monoclonal IgM antibodies. 858 F.2d at 734. Prior to Wands, most immunoassays used IgG isotype. IgM were disfavored because of their sensitivity to reducing agents and their tendency to self-aggregate and precipitate. Id. The position of the PTO was that the production of high-affinity IgM anti-HbsAg antibodies was unpredictable and unreliable, and therefore, the PTO asserted that it would require undue experimentation to make the antibodies. 858 F.2d at 735.

The Federal Circuit Court reversed the PTO's rejection of Wands' claims as being not enabling. The Court reasoned that undue experimentation would not be required to practice the invention when the "disclosure provides considerable direction and guidance on how to practice their invention and presents working examples" and there is "high level of skill in the art at the time the application was filed" and "all of the methods needed to practice the invention were well known". 858 F.2d at 740. Furthermore, "it seems unlikely that undue experimentation would be defined in terms of the number of" experiments. Id. A considerable amount of experimentation is permissible, if it is merely routine. 858 F.2d at 737.

The present invention is in parallel with Wands. The position of the Final Office Action is that one skilled in the art would expect sperm-specific antibodies to inhibit fertilization but not to retain the ability of fertilization. The Final Office Action then asserts that it would require undue experimentation to expect that the claimed antibodies would retain the ability to fertilize oocytes.

As discussed in Section (I)(a) of this communication, Applicant has pointed out that one skilled in the art would not expect that all sperm-specific antibodies would inhibit fertilization. Actually, some sperm-specific antibodies clearly do not. *See*, Chiu & Chamley.

Applicant notes that the present application is a continuation-in-part of Application No. 09/537,861 (the '861 Application). In the `861 Application, Applicant

provides considerable direction and guidance in making and screening sperm-specific antibodies. The procedure entails immunizing mice with mouse sperm cells and screening sperm-binding antibodies with flow cytometry (See Example I of the `861 Application). Applicant also teaches that, to determine whether the sperm binding antibodies would not inhibit fertilization, sperm cells bound with the antibodies may be incubated with oocytes and resulting zygotes may then be cultured into blastocytes which are readily observable. (Example III of the present application) It is common knowledge that if the fertilization is inhibited no blastocyte will be formed or observed. Put together, Applicant provides considerable direction and guidance on how to practice claimed invention by making antibodies that bind to a sperm cell and retain the sperm cell's ability to fertilize an oocyte.

Furthermore, Applicant presents a working example. Applicants have identified mAbC as one embodiment of the claimed antibodies.

Finally, Applicant notes that all the methods to practice claimed invention are well known and routine in the art.

In light of the rulings of Wands, Applicant finds no reason that it would require undue experimentation to make and/or use the claimed antibodies, much less to expect that the claimed antibodies would retain the ability to fertilize an oocyte.

II. Biological materials need not be deposited.

37 CFR § 1.802 states in pertinent part that "biological materials need not be deposited, *inter alia*, if it is known and readily available to the public or can be made or isolated without undue experimentation". However, a deposit has been held necessary where the starting materials are not readily available to the public. Even when starting materials are available, a deposit has been necessary where it would require undue experimentation to make the claimed invention from the starting material. In re Wands, 858 F.2d at 735.

In the present application, the starting materials to make the claimed antibodies are sperm cells of a species, which are readily available in the public. As discussed in Section I(b), the claimed antibodies can be made without undue experimentation from the starting materials. Accordingly, biological materials in the present invention need not be deposited.